EXHIBIT

19

DEFENDANTS' MOTION TO EXCLUDE THE TESTIMONY OF DR. CHRISTOPHER TEAF

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Reference Manual on Scientific Evidence

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Summary Table of Contents

A detailed Table of Contents appears at the front of each chapter

including such details as the number of animals per cage, dose and chemical verification, and the handling of tissue specimens. GLP practices are remarkably similar across agencies, but the tests called for differ depending on mission. For example, there are major differences between the FDA's and the EPA's required procedures for testing drugs and environmental chemicals.[30] The FDA requires and specifies both efficacy and safety testing of drugs in humans and animals. Carefully controlled clinical trials using doses within the expected therapeutic range are required for premarket testing of drugs because exposures to prescription drugs are carefully controlled and should not exceed specified ranges or uses. However, for environmental chemicals and agents, no premarket testing in humans is required by the EPA. Moreover, since exposures are less predictable, a wider range of doses usually is given in the animal tests.[31]

Since exposures to environmental chemicals may continue over the lifetime and affect both young and old, test designs called lifetime bioassays have been developed in which relatively high doses are given to experimental animals. Interpretation of results requires extrapolation from animals to humans, from high to low doses, and from short exposures to multiyear estimates. It must be emphasized that less than 1% of the 60,000–75,000 chemicals in commerce have been subjected to a full safety assessment, and there are significant toxicological data on only 10%–20%.

Risk assessment is an approach increasingly used by regulatory agencies to estimate and compare the risks of hazardous chemicals and to assign priority for avoiding their adverse effects.[32] The National Academy of Sciences defines four components of risk assessment: hazard identification, dose–response estimation, exposure assessment, and risk characterization.[33]

Although risk assessment is not an exact science, it should be viewed as a

safety of consumer products is described in *United States v. Keplinger,* 776 F.2d 678 (7th Cir. 1985), *cert. denied,* 476 U.S. 1183 (1986). Keplinger and the other defendants in this case were toxicologists who were convicted of falsifying data on product safety by underreporting animal morbidity and mortality and omitting negative data and conclusions from their reports.

30. *See, e.g.,* 40 C.F.R. §§ 160, 792 (1993); Lu, *supra* note 14, at 89.

31. It must be appreciated that the development of a new drug inherently requires searching for an agent that at useful doses has a biological effect (e.g., decreasing blood pressure), whereas those developing a new chemical for consumer use (e.g., a house paint) hope that at usual doses no biological effects will occur. There are other compounds, such as pesticides and antibacterial agents, for which a biological effect is desired, but it is intended that at usual doses humans will not be affected. These different expectations are part of the rationale for the differences in testing information available for assessing toxicological effects.

32. Committee on Risk Assessment Methodology, National Research Council, *supra* note 19, at 1.

33. *See generally* National Research Council, Risk Assessment in the Federal Government: Managing the Process (1983); Bernard D. Goldstein, *Risk Assessment/Risk Management Is a Three-Step Process: In Defense of EPA's Risk Assessment Guidelines,* 7 J. Am. C. Toxicol. 543 (1988); Bernard D. Goldstein, *Risk Assessment and the Interface Between Science and Law,* 14 Colum. J. Envtl. L. 343 (1989).

useful estimate on which policy making can be based. In recent years, codification of the methodology used to assess risk has increased confidence that the process can be reasonably free of bias; however, significant controversy remains, particularly when actual data are limited and generally conservative default assumptions are used.[34]

While risk assessment information about a chemical can be somewhat useful in a toxic tort case, at least in terms of setting reasonable boundaries as to the likelihood of causation, the impetus for the development of risk assessment has been the regulatory process, which has different goals.[35] Because of their use of appropriately prudent assumptions in areas of uncertainty and their use of default assumptions when there are limited data, risk assessments intentionally encompass the upper range of possible risks.

F. Toxicology and Epidemiology

Epidemiology is the study of the incidence and distribution of disease in human populations. Clearly, both epidemiology and toxicology have much to offer in elucidating the causal relationship between chemical exposure and disease.[36] These sciences often go hand in hand in assessments of the risks of chemical exposure, without artificial distinctions being drawn between them. However, although courts generally rule epidemiological expert opinion admissible, admissibility of toxicological expert opinion has been more controversial because of uncertain-

34. An example of conservative default assumptions can be found in Superfund risk assessment. The EPA has determined that Superfund sites should be cleaned up to reduce cancer risk from 1 in 10,000 to 1 in 1,000,000. A number of assumptions can go into this calculation, including conservative assumptions about intake, exposure frequency and duration, and cancer-potency factors for the chemicals at the site. *See, e.g.,* Robert H. Harris & David E. Burmaster, *Restoring Science to Superfund Risk Assessment,* 6 Toxics L. Rep. (BNA) 1318 (Mar. 25, 1992).

35. *See, e.g.,* Ellen Relkin, *Use of Governmental and Industrial Standards of Exposure and Toxicological Data in Toxic Tort Litigation, reprinted in* Proving Causation of Disease: Update 1996, at 199 (New Jersey Inst. for Continuing Legal Educ. 1996); Steven Shavell, *Liability for Harm Versus Regulation of Safety,* 13 J. Legal Stud. 357 (1984). Risk assessment has been heavily criticized on a number of grounds. The major argument of industry has been that it is overly conservative and thus greatly overstates the actual risk. The rationale for conservatism is in part the prudent public health approach of "above all, do no harm." The conservative approach is also used, especially in regard to cancer risk, because it is sometimes more feasible to extrapolate to a plausible upper boundary for a risk estimate than it is to estimate a point of maximum likelihood. For a sample of the debate over risk assessment, see Bruce N. Ames & Lois S. Gold, *Too Many Rodent Carcinogens: Mitogenesis Increases Mutagenesis,* 249 Science 970 (1990); Jean Marx, *Animal Carcinogen Testing Challenged,* 250 Science 743 (1990); Philip H. Abelson, *Incorporation of a New Science into Risk Assessment,* 250 Science 1497 (1990); Frederica P. Perera, *Letter to the Editor: Carcinogens and Human Health, Part 1,* 250 Science 1644 (1990); Bruce N. Ames & Lois S. Gold, *Response,* 250 Science 1645 (1990); David P. Rall, *Letter to the Editor: Carcinogens and Human Health, Part 2,* 251 Science 10 (1991); Bruce N. Ames & Lois S. Gold, *Response,* 251 Science 12 (1991); John C. Bailar III et al., *One-Hit Models of Carcinogenesis: Conservative or Not?,* 8 Risk Analysis 485 (1988).

36. *See* Michael D. Green et al., Reference Guide on Epidemiology § V, in this manual.